

Heller Ehrman LLP  
Attorney Docket No. 40923-0079 US3

U.S. Serial No. 09/965,796  
INVENTOR: David M. GOLDENBERG

**Amendments to the Claims:**

The below listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

1. to 23. (Canceled).

24. (Currently Amended) A method for treating a subject having a B-cell malignancy, comprising administering to the subject a therapeutic composition comprising a pharmaceutically acceptable carrier, and an immunoconjugate, wherein the immunoconjugate comprises

(i) at least one human, humanized or chimeric anti-CD22 antibody or a fragment thereof,

**wherein the antibody fragment is selected from the group consisting of F(ab')<sub>2</sub>, Fab', Fab, and single chain Fv, and**

(ii) a drug, ~~a toxin, an immunomodulator, a chelator, a boron compound, a photoactive agent or dye,~~ or a radioisotope, wherein said radioisotope is other than <sup>131</sup>I, **wherein the immunoconjugate is used in combination with a naked anti-CD20 mab.**

25. (Previously Presented) The method according to claim 24, wherein the immunoconjugate comprises a chemotherapeutic drug.

26. (Previously Presented) The method according to claim 25, wherein the chemotherapeutic drug is selected from the group consisting of cyclophosphamide, etoposide, vincristine, procarbazine, prednisone, carmustine, doxorubicin, methotrexate, bleomycin, dexamethasone, phenyl butyrate, bryostatin-1 and leucovorin.

27. (Previously Presented) The method according to claim 25, wherein the chemotherapeutic drug is selected from the group consisting of nitrogen mustards, alkyl sulfonates, nitrosoureas, triazines, folic acid analogs, pyrimidine analogs, purine analogs, antibiotics, epipodophyllotoxins, platinum coordination complexes, and hormones.

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28-35. (Canceled)

36. (Currently Amended) The method according to claim 2425, wherein the anti-CD22 antibody or fragment thereof is a human antibody-or antibody fragment.

37. (Currently Amended) The method according to claim 2425, wherein the anti-CD22 antibody or fragment thereof is a humanized antibody or antibody fragment.

38. (Currently Amended) The method according to claim 2425, wherein the anti-CD22 antibody or fragment thereof is a chimeric antibody or antibody fragment.

39. (Currently Amended) The method according to claim 2425, wherein the anti-CD22 antibody or fragment thereof comprises a multivalent fusion protein that additionally comprises at least one antibody component that binds with CD19, CD20, CD52 or CD74.

40. (Previously Presented) The method according to claim 39, wherein the anti-CD22 antibody or fragment thereof comprises a trivalent fusion protein.

41. (Previously Presented) The method according to claim 39, wherein the anti-CD22 antibody or fragment thereof comprises a tetravalent fusion protein.

42. (Previously Presented) The method according to claim 39, wherein the anti-CD22 antibody or fragment thereof comprises a pentavalent fusion protein.

43. (Previously Presented) The method according to claim 24, wherein the immunoconjugate comprises polyethyleneglycol to extend the half-life of the antibody or fragment thereof, in blood, lymph, or other extracellular fluids.

44. (Previously Presented) The method according to claim 24, wherein the anti-CD22 antibody-or antibody fragment is a human antibody or antibody fragment.

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45. (Previously Presented) The method according to claim 24, wherein the anti-CD22 antibody-or antibody fragment is a single chain Fv antibody fragment comprising  $V_H$  and  $V_L$  chains are connected by a peptide linker.

46. (Canceled)

47. (Previously Presented) The method according to claim 24, wherein the therapeutic composition comprises at least two monoclonal antibodies that bind with distinct CD22 epitopes, wherein the CD22 epitopes are selected from the group consisting of epitope A, epitope B, epitope C, epitope D and epitope E.

48-51. (Canceled)

52. (Currently Amended) The method according to claim ~~24~~50, wherein the radioisotope is selected from the group consisting of  $^{198}\text{Au}$ ,  $^{32}\text{P}$ ,  $^{125}\text{I}$ ,  $^{90}\text{Y}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{67}\text{Cu}$ ,  $^{211}\text{At}$ ,  $^{213}\text{Bi}$ , and  $^{224}\text{Ac}$ .

53-54. (Canceled)

55. (Currently Amended) The method according to claim ~~24~~54, wherein the anti-CD22 immunoconjugate comprises a  $^{90}\text{Y}$  radioisotope.

56. (Previously Presented) The method according to claim 55, wherein the  $^{90}\text{Y}$  is attached to the anti-CD22 immunoconjugate by means of chelating agent.

57. (Previously Presented) The method according to claim 56, wherein the chelating agent is diethylenetriaminepentaacetic acid.

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58. (Previously Presented) The method according to claim 38, wherein the radioisotope is  $^{67}\text{Cu}$ .

59. (Previously Presented) The method according to claim 58, wherein the chelating agent is p-bromoacetamido-benzyl-tetraethylaminetetraacetic acid.

60. (Currently Amended) A method for treating a subject having a B-cell malignancy, comprising administering to the subject a therapeutic composition comprising a pharmaceutically acceptable carrier, and an immunoconjugate, wherein the immunoconjugate comprises

(i) at least one human, humanized or chimeric anti-CD22 antibody or a fragment thereof, wherein the antibody fragment is selected from the group consisting of F(ab')<sub>2</sub>, Fab', Fab, and single chain Fv, and

(ii) a therapeutic agent selected from the group consisting of a drug, ~~a toxin, an immunomodulator, a boron compound, a photoactive agent or dye~~, and a radioisotope, wherein the therapeutic agent is attached indirectly via a linkage to the anti-CD22 antibody or antibody fragment or is attached directly to the anti-CD22 antibody or antibody fragment-via a free sulfhydryl group.

61. (Previously Presented) The method according to claim 60, wherein the therapeutic agent is attached ~~indirectly via an aminodextran~~ indirectly via a polypeptide carrier to the anti-CD22 antibody or antibody fragment ~~via an aminodextran that is attached to the anti-CD22 antibody or antibody fragment~~.

62. (Previously Presented) The method according to claim 61, wherein the therapeutic agent is attached ~~indirectly via a polypeptide carrier~~ indirectly via a polypeptide carrier to the anti-CD22 antibody or antibody fragment ~~via a polypeptide carrier that is attached to the anti-CD22 antibody or antibody fragment~~.

63. (Previously Presented) The method according to claim 62, wherein the therapeutic agent is a radioisotope.

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64. (Previously Presented) The method according to claim 63, wherein the radioisotope is selected from the group consisting of  $^{198}\text{Au}$ ,  $^{32}\text{P}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{90}\text{Y}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{67}\text{Cu}$ ,  $^{211}\text{At}$ ,  $^{213}\text{Bi}$ , and  $^{224}\text{Ac}$ .

65. (Previously Presented) The method according to claim 63, wherein the radioisotope is  $^{131}\text{I}$ .

66. (Previously Presented) The method according to claim 63, wherein the radioisotope is  $^{90}\text{Y}$ .

67. (Previously Presented) The method according to claim 60, wherein the therapeutic agent is a radioisotope that is attached indirectly to the anti-CD22 antibody or antibody fragment via a chelating agent.

68. (Previously Presented) The method according to claim 67, wherein the radioisotope is selected from the group consisting of  $^{198}\text{Au}$ ,  $^{32}\text{P}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{90}\text{Y}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{67}\text{Cu}$ ,  $^{211}\text{At}$ ,  $^{213}\text{Bi}$ , and  $^{224}\text{Ac}$ .

69. (Previously Presented) The method according to claim 68, wherein the radioisotope is  $^{131}\text{I}$ .

70. (Previously Presented) The method according to claim 68, wherein the radioisotope is  $^{90}\text{Y}$ .

71. (Previously Presented) The method according to claim 67, wherein the chelating agent is p-bromoacetamido-benzyl-tetraethylaminetetraacetic acid.

72. (Previously Presented) The method according to claim 71, wherein the radioisotope is  $^{67}\text{Cu}$ .

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73. (Previously Presented) The method according to claim 67, wherein the chelating agent is diethylenetriaminepentaacetic acid.

74. (Previously Presented) The method according to claim 73, wherein the radioisotope is  $^{90}\text{Y}$ .

75. (Previously Presented) The method according to claim 70, wherein the therapeutic agent is attached directly to the anti-CD22 antibody or antibody fragment by means of a free sulfhydryl group.

76. (Previously Presented) The method according to claim 75, wherein the therapeutic agent is a radioisotope.

77. (Previously Presented) The method according to claim 76, wherein the radioisotope is selected from the group consisting of  $^{198}\text{Au}$ ,  $^{32}\text{P}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{90}\text{Y}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{67}\text{Cu}$ ,  $^{211}\text{At}$ ,  $^{213}\text{Bi}$ , and  $^{224}\text{Ac}$ .

78. (Previously Presented) The method according to claim 77, wherein the radioisotope is  $^{131}\text{I}$ .

79. (Previously Presented) The method according to claim 77, wherein the radioisotope is  $^{90}\text{Y}$ .

80. (Previously Presented) The method according to claim 75, wherein the therapeutic agent is attached directly to a free sulfhydryl group at the hinge region of a reduced antibody component via disulfide bond formation.

81. (Previously Presented) The method according to claim 80, wherein the therapeutic agent is a radioisotope.

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82. (Previously Presented) The method according to claim 81, wherein the radioisotope is selected from the group consisting of  $^{198}\text{Au}$ ,  $^{32}\text{P}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{90}\text{Y}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{67}\text{Cu}$ ,  $^{211}\text{At}$ ,  $^{213}\text{Bi}$ , and  $^{224}\text{Ac}$ .

83. (Previously Presented) The method according to claim 82, wherein the radioisotope is  $^{131}\text{I}$ .

84. (Previously Presented) The method according to claim 82, wherein the radioisotope is  $^{90}\text{Y}$ .

85. (Presently Presented) The method according to claim 80, wherein the therapeutic agent is attached indirectly to the anti-CD22 antibody or antibody fragment by means of an aminodextran, a polypeptide carrier or a chelating agent that is attached to the anti-CD22 antibody or antibody fragment through an oxidized antibody component.

86. (Presently Presented) The method according to claim 80, wherein the therapeutic agent is attached indirectly to an anti-CD22 antibody fragment via a carbohydrate moiety introduced into the light chain variable region of the antibody fragment.

87. (Presently Presented) The method according to claim 85, wherein the therapeutic agent is a radioisotope.

88. (Presently Presented) The method according to claim 87, wherein the radioisotope is  $^{90}\text{Y}$ .

89. (Presently Presented) The method according to claim 87, wherein the radioisotope is  $^{131}\text{I}$ .

90. (Canceled)

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91. (Presently Presented) The method according to claim 60, wherein the anti-CD22 antibody or antibody fragment is a humanized antibody or antibody fragment.

92. (Presently Presented) The method according to claim 60, wherein the anti-CD22 antibody or antibody fragment is a chimeric antibody or antibody fragment.

93. (Presently Presented) The method according to claim 60, wherein the anti-CD22 antibody or antibody fragment is a murine antibody or antibody fragment.

94. (Presently Presented) The method according to claim 60, wherein the therapeutic agent is  $^{131}\text{I}$  in a dose of 15 to 40 mCi.

95. (Presently Presented) The method according to claim 94, wherein the dose is 20 to 30 mCi.

96. (Presently Presented) The method according to claim 60, wherein the therapeutic agent is  $^{90}\text{Y}$  in a dose of 10 to 30 mCi.

97. (Presently Presented) The method according to claim 96, wherein the dose is 10 to 20 mCi.